Overview of Antidepressants

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How they work

- They somehow affect one of three neurotransmitters: serotonin, norepinephrine, or dopamine.
- The change at the neuronal junction is usually immediate, but efficacy lags for several weeks corresponding with down regulation of postsynaptic receptors.
- Not totally understood: G proteins, second messengers, and gene expression.

Indications for Use

- Major Depression
- Dysthymia
- OCD
- Panic Disorder
- Bulimia
- Social Phobia
- PTSD
- Irritable Bowel Syndrome
- Migraine Headaches
- Enuresis
- ADHD
- Smoking Cessation
- Autism
- Late Luteal Phase Dysphoric Disorder

Functional Groupings

- Tricyclic and Heterocyclic Antidepressants
- Selective Serotonin Reuptake Inhibitors
- Monoamine Oxidase Inhibitors
- “Grab Bag”- Miscellaneous

TCA's

- Most Common uses: Chronic Pain, OCD, Migraines, and refractory Depression
- Receptors: Serotonin, Norepinephrine, small amount of Dopamine
- Other receptors: alpha-1 blockade, muscarinic cholinergic receptors, H-1 histamine, sodium channels in the heart

TCA Dosing

- Most TCA's
  - start at 25-50mg
  - increase by 75-100mg a week as tolerated
  - target is around 300mg
- Nortriptyline
  - start at 25mg
  - increase to target of 75mg over 1-2 weeks

Side Effects of TCA's

- 5HT-2 = sexual dysfunction, anxiety, insomnia, agitation, tremor
- 5HT-3 = GI side effects
- Anticholinergic = blurred vision (glaucoma), dry mouth, constipation, urinary retention, tachycardia, and delirium
- Antihistamine = sedation, weight gain
- Alpha-1 blockade = orthostatic hypotension

Precautions for TCA's

- Cardiac effects = Na channel blockade
- All patients >40 need EKG before starting
- Overdose:
  - Ventricular Arrhythmias = Lidocaine
  - QRS longer than 120 msec = phenytoin or pace-maker
- Therapeutic monitoring - not needed for most patients
- Significant 2D6 P450 interactions

SSRI's

- Most common uses: Depression, OCD, Panic disorder, Bulimia
- Receptors: Serotonin
- 5HT-1 = Efficacy, "where the money is"
- 5HT-2 = sexual dysfunction, anxiety, insomnia, agitation, tremor
- 5HT-3 = GI side effects
- Increased serotonin decreases Dopamine = lack of sexual desire

SSRI Dosing

- Prozac
  - start at 20mg, therapeutic range 20-80
- Zoloft
  - start at 50mg, therapeutic range 50-200mg
- Paxil
  - start at 20mg, therapeutic range 20-60mg
- Celexa
  - start at 20mg, therapeutic range 20-60mg

Pearls

- Prozac: 1/2 life 72hrs, high P450 interactions, activating
- Zoloft: 1/2 life 26hrs, low P450 interactions, high GI effects
- Paxil: 1/2 life 20hrs, high P450 interactions, anticholinergic
- Celexa: 1/2 life 35 hrs, low P450 interactions

Pearls cont.

- All short half life SSRI's will have discontinuation syndrome.
- When added with other serotonin active medications can have serotonin syndrome
- Luvox less popular but used for OCD
- Generally safe in overdose
- No cardiac effects

MAOI’s

- Receptors: block monoamine oxidase which increases levels of norepinephrine, serotonin, and dopamine
- Not common due to: dietary restrictions, drug interactions, side effects, hypertensive crisis
- Used for atypical depression

“Grab Bag”

- Effexor
  - Indications: Depression, GAD, ?chronic pain?
  - Receptors: Serotonin, Norepinephrine, Dopamine -Add as you increase the dose
  - Side effects: 5HT-2/3, ?blood pressure
  - Dosing: start at 37.5mg QD and increase to 75-225mg QD, can go up to 375mg QD
  - Low P450, Lowest protein binding

“Grab Bag” cont.

- Wellbutrin
  - Indications: Depression, ADHD, Smoking cessation
  - Receptors: Norepinephrine and Dopamine
  - Side effects: Headache, insomnia, agitation, GI upset
  - Dosing: SR 150mg qd for 1 week, then SR 150 BID
  - No sexual side effects!, LOW P450 (2B6)

“Grab Bag” cont.

- Serzone
  - Indications: Depression
  - Receptors: Serotonin, Blocks 5HT-2
  - Side effects: sedation, nausea, dizziness, blurred vision (no significant Histamine or cholinergic blockade)
  - Dosing: 50mg qhs titrate to 300-600mg BID
  - No sexual side effects!, Good for insomnia, high interactions with P450 3A-3/4

“Grab Bag” cont.

- Trazadone
  - Bad antidepressant, but good for sleep, Priapism!
- Remeron
  - Blocks Alpha-2, blocks 5HT-2/3, antihistamine
  - Low P450, Sedation and weight gain, can elevate lipid levels.
  - No sexual side effects!

Matching Patients to Medications

- 20 y/o female with Bulemia
- SSRI
- 30 y/o male trying to conceive
- Wellbutrin, Serzone, why not SSRI
- 19 y/o male, anxiety disorder, premature ejaculation
- Effexor, SSRI

Matching Patients to Medications

- 75 y/o male taking coumadin and 10 other medications with depression and anxiety
- Celexa, Effexor, Zoloft
- Why not TCA, Wellbutrin, Serzone

Matching Patients to Medications

- 50 y/o male with Chronic pain and Depression
- TCA or ?Effexor
- He also has OCD
- Clomipramine
- He comes in for an acute appointment with a painful red eye, palpitations, and shortness of breath.

Questions?